

General

Guideline Title

Guideline for the prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer patients.

Bibliographic Source(s)

Dupuis LL, Boodhan S, Holdsworth M, Robinson PD, Hain R, Portwine C, O'Shaughnessy E, Sung L. Guideline for the prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer patients. Toronto (ON): Pediatric Oncology Group of Ontario (POGO); 2012. 199 p. [129 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Strength of recommendations (Strong, Weak) and quality of evidence (High, Moderate, Low, Very Low) are defined at the end of the "Major Recommendations" field.

Note: Emetogenicity (emetic potential) referenced throughout the recommendations is defined as:

- *High emetic potential: greater than 90% frequency of emesis in the absence of effective prophylaxis*
- *Moderate emetic potential: 30 to 90% frequency of emesis in the absence of effective prophylaxis*
- *Low emetic potential: 10 to less than 30% frequency of emesis in the absence of effective prophylaxis*
- *Minimal emetic potential: less than 10% frequency of emesis in the absence of effective prophylaxis*

1. How is optimal control of acute antineoplastic-induced nausea and vomiting (AINV) defined?

The Panel recommends that optimal control of acute AINV be defined as no vomiting, no retching, no nausea, no use of antiemetic agents other than those given for AINV prevention and no nausea-related change in the child's usual appetite and diet. This level of AINV control is to be achieved on each day that antineoplastic therapy is administered and for 24 hours after administration of the last antineoplastic agent of the antineoplastic therapy block. (Strong recommendation, Very low quality evidence)

2a. What pharmacological interventions provide optimal control of acute AINV in children receiving antineoplastic agents of high emetic risk?

The Panel recommends that:

- Children ≥ 12 years old and receiving antineoplastic agents of high emetic risk which are not known or suspected to interact with aprepitant receive: *ondansetron or granisetron + dexamethasone + aprepitant* (Strong recommendation, Very low quality evidence)

- Children ≥ 12 years old and receiving antineoplastic agents of high emetic risk which are known or suspected to interact with aprepitant receive: *ondansetron or granisetron + dexamethasone* (Strong recommendation, Moderate quality evidence)
- Children < 12 years old and receiving antineoplastic agents of high emetic risk receive: *ondansetron or granisetron + dexamethasone* (Strong recommendation, Moderate quality evidence)

2b. What pharmacological interventions provide optimal control of acute AINV in children receiving antineoplastic agents of moderate emetic risk?

The Panel recommends that children receiving antineoplastic agents of moderate emetogenicity receive: *ondansetron or granisetron + dexamethasone* (Strong recommendation, Moderate quality evidence)

2c. What pharmacological interventions provide optimal control of acute AINV in children receiving antineoplastic agents of low emetic risk?

The Panel recommends that children receiving antineoplastic agents of low emetic risk receive: *ondansetron or granisetron* (Strong recommendation, Moderate quality evidence)

2d. What pharmacological interventions provide optimal control of acute AINV in children receiving antineoplastic agents of minimal emetic risk?

The Panel recommends that children receiving antineoplastic agents of low emetic risk receive: *no routine prophylaxis* (Strong recommendation, Very low quality evidence)

3. What adjunctive non-pharmacological interventions provide control of acute AINV in children receiving antineoplastic agents of any emetic risk?

The Panel suggests that acupuncture, acupressure, guided imagery, music therapy, progressive muscle relaxation and psycho-educational support and information may be effective in children receiving antineoplastic agents. Virtual reality may convey benefit. (Weak recommendation, Very low quality evidence)

The Panel suggests that the following dietary interventions may be effective:

- Eat smaller, more frequent meals
- Reduce food aromas and other stimuli with strong odours
- Avoid foods that are spicy, fatty or highly salty
- Take antiemetics prior to meals so that the effect is present during and after meals
- Measures and foods (e.g., "comfort foods") that helped to minimize nausea in the past

(Weak recommendation, Very low quality evidence)

4. What is the role of aprepitant in children receiving antineoplastic therapy?

The Panel recommends that the use of aprepitant be restricted to children 12 years of age and older who are about to receive highly emetogenic antineoplastic therapy which is not known or suspected to interact with aprepitant. There is no evidence to support the safe and effective use of aprepitant in younger children. (Strong recommendation, Very low quality evidence)

5. What pharmacological interventions provide optimal control of acute AINV in children receiving highly or moderately emetogenic antineoplastic agents in whom corticosteroids are contraindicated?

The Panel suggests that children receiving highly emetogenic antineoplastic therapy who cannot receive corticosteroids receive: *ondansetron or granisetron + chlorpromazine, or nabilone* (Weak recommendation, Low quality evidence)

The Panel suggests that children receiving moderately emetogenic antineoplastic therapy who cannot receive corticosteroids receive: *ondansetron or granisetron + chlorpromazine, or metoclopramide, or nabilone* (Weak recommendation, Low quality evidence)

6. What doses of antiemetic agents are known to be effective in children receiving antineoplastic agents?

The Panel recommends the following aprepitant dose for children 12 years of age and older: *Day 1: 125mg by mouth (PO) x 1; Days 2 and 3: 80mg PO once daily* (Strong recommendation, Moderate quality evidence)

The Panel recommends the following chlorpromazine dose: *0.5mg/kg/dose IV q6h* (Strong recommendation, Low quality evidence)

The Panel suggests the following dexamethasone for children receiving highly emetogenic antineoplastic therapy: *6 mg/m²/dose IV/PO q6h*

If given concurrently with aprepitant, reduce dexamethasone dose by half. (Weak recommendation, Low quality evidence)

The Panel recommends the following dexamethasone for children receiving moderately emetogenic antineoplastic therapy:

- $\leq 0.6 \text{ m}^2$: 2mg/dose IV/PO q12h
- $> 0.6 \text{ m}^2$: 4mg/dose IV/PO q12h

If given concurrently with aprepitant, reduce dexamethasone dose by half. (Strong recommendation, Low quality evidence)

The Panel recommends the following IV granisetron dose for children receiving highly emetogenic antineoplastic therapy: 40 mcg/kg/dose IV as a single daily dose (Strong recommendation, Low quality evidence)

The Panel recommends the following IV granisetron dose for children receiving moderately emetogenic antineoplastic therapy: 40 mcg/kg/dose IV as a single daily dose (Strong recommendation, Moderate quality evidence)

The Panel suggests the following oral granisetron dose for children receiving moderately emetogenic antineoplastic therapy: 40 mcg/kg/dose PO q12h (Weak recommendation, Low quality evidence)

The Panel recommends the following IV granisetron dose for children receiving antineoplastic therapy of low emetogenicity: 40 mcg/kg/dose IV as a single daily dose (Strong recommendation, Low quality evidence)

The Panel suggests the following oral granisetron dose for children receiving antineoplastic therapy of low emetogenicity: 40 mcg/kg/dose PO q12h (Weak recommendation, Low quality evidence)

The Panel recommends the following metoclopramide dose for children receiving moderately emetogenic antineoplastic therapy: 1 mg/kg/dose IV pre-therapy x 1 then 0.0375 mg/kg/dose PO q6h

Give diphenhydramine or benztropine concurrently (Strong recommendation, Low quality evidence)

The Panel suggests the following nabilone dose:

- $< 18 \text{ kg}$: 0.5 mg/dose PO twice daily
- 18 to 30 kg: 1 mg/dose PO twice daily
- $> 30 \text{ kg}$: 1 mg/dose PO three times daily
- Maximum: 0.06 mg/kg/day

(Weak recommendation, Low quality evidence)

The Panel recommends the following ondansetron dose for children receiving highly emetogenic antineoplastic therapy: 5 mg/m²/dose (0.15 mg/kg/dose) IV/PO pre-therapy x 1 and then q8h (Strong recommendation, Moderate quality evidence)

The Panel recommends the following ondansetron dose for children receiving moderately emetogenic antineoplastic therapy: 5 mg/m²/dose (0.15 mg/kg/dose; maximum 8 mg/dose) IV/PO pre-therapy x 1 and then q12h (Strong recommendation, Moderate quality evidence)

The Panel recommends the following ondansetron dose for children receiving therapy of low emetogenicity: 10 mg/m²/dose (0.3 mg/kg/dose; maximum 16 mg/dose IV or 24 mg/dose PO) pre-therapy x 1 (Strong recommendation, Low quality evidence)

Definitions:

Quality of Evidence

High quality - Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality - Any estimate of effect is very uncertain

Strength of Recommendations

Strength of Recommendation	Benefit vs Risk and Burdens	Methodology	Implications
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Strength of Recommendation	Desirable Effects vs. Risks and Burdens	Evidence Methodology	Implications
Strong recommendation, high quality evidence	Desirable effects clearly outweigh undesirable effects or <i>vice versa</i>	randomized controlled trials (RCTs) or Exceptional observational studies	Apply to most circumstances Further research unlikely to change recommendation
1B Strong recommendation, moderate quality evidence	Desirable effects clearly outweigh undesirable effects or <i>vice versa</i>	Evidence from RCTs with some flaws in study or Very strong evidence from observational studies	Apply to most patients in most circumstances Further research might be helpful
1C Strong recommendation, poor quality evidence	Desirable effects clearly outweigh undesirable effects or <i>vice versa</i>	Evidence of at least one critical outcome from observational studies, case series or RCTs with flaws	Apply to most patients in many circumstances Further research would be helpful
2A Weak recommendation, high quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important flaws or Exceptionally strong evidence from observational studies	Best action may depend on circumstances or patient or society values Further research unlikely to change recommendation
2B Weak recommendation, moderate quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important flaws or Very strong evidence from observational studies	Best action dependent on patient circumstances or patient or society values Further research may change recommendation
2C Weak recommendation with poor quality evidence	Desirable effects closely balanced with undesirable effects	Evidence of at least one critical outcome from observational studies, case series or RCTs with serious flaws	Other alternatives may be equally reasonable Further research very likely to change recommendation

Clinical Algorithm(s)

A clinical algorithm for selection of antiemetics is provided in Appendix L of the original guideline document.

Scope

Disease/Condition(s)

Acute antineoplastic-induced nausea and vomiting (AINV)

Note: The scope of this guideline is limited to the prevention of AINV in the acute phase (within 24 hours of administration of an antineoplastic agent). Its scope does not include anticipatory, breakthrough or delayed phase AINV, or nausea and vomiting that is related to radiation therapy, disease, co-incident conditions or end-of-life care.

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Risk Assessment

Treatment

Clinical Specialty

Gastroenterology

Oncology

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To provide physicians, nurses, pharmacists and other health care providers who care for children aged 1 month to 18 years who are receiving antineoplastic medication with an approach to the prevention of acute antineoplastic-induced nausea and vomiting (AINV).
- To facilitate the selection of interventions, including pharmacological, non-pharmacological and complementary interventions (e.g., homeopathy, herbal, acupressure), which will provide optimal control of acute AINV in children with cancer receiving antineoplastic therapy including those undergoing conditioning for hematopoietic stem cell transplant (HSCT).
- To reduce the impact of inconsistent antiemetic prophylaxis on patients and families, especially those who receive care at more than one facility.

Target Population

Children aged 1 month to 18 years who are receiving antineoplastic medication

Note: This guideline is most applicable to children who are naïve to antineoplastic therapy and who are about to receive their first course of antineoplastic therapy.

Interventions and Practices Considered

1. Antiemetic agents
 - Ondansetron
 - Granisetron

- Dexamethasone
- Aprepitant (for ages 12 and older)
- Nabilone
- Chlorpromazine
- Metoclopramide

2. Adjunctive therapy

- Acupuncture
- Acupressure
- Guided imagery
- Music therapy
- Progressive muscle relaxation
- Psycho-educational support and information

3. Dietary interventions

- Smaller, more frequent meals
- Reduce food aromas
- Avoid spicy, fatty or highly salty foods
- Take antiemetics prior to meal
- Measures and foods that minimize nausea

Major Outcomes Considered

Optimal control of acute antineoplastic-induced nausea and vomiting (AINV)

Note: Optimal control of acute AINV is defined by the Panel as no vomiting, no retching, no nausea, no use of antiemetic agents other than those given for AINV prevention and no nausea-related change in the child's usual appetite and diet. This level of AINV control is to be achieved on each day that antineoplastic therapy is administered and for 24 hours after administration of the last antineoplastic agent of the antineoplastic therapy block.

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Identification and Appraisal of Existing Guidelines

A guideline was sought which could be adapted to the Pediatric Oncology Group of Ontario (POGO) context for acute antineoplastic-induced nausea and vomiting (AINV) prevention.

(a) Guideline Search Strategy: In February 2010, the POGO AINV Guideline Development Group conducted a comprehensive literature search and environmental scan to identify existing practice guidelines for the management of acute antineoplastic induced nausea and vomiting for children and youth with cancer. Computerized searches were performed with the assistance of a library scientist using the OVID search platform in the following databases: Medline, Embase, Cochrane Central Register of Controlled Trials (CCTR), Allied and Complementary Medicine (AMED), Health Technology Assessment (HTA) and NHS Economic Evaluation Database (NHSEED) as well as the EBSCOhost information provider in the CINHALL database. The search engine Google was utilized for identification of grey literature including local, provincial, national and international databases. Personal files of panel members were also reviewed for papers that merited inclusion in our results. In addition, panel members identified guidelines for prevention of AINV for pediatric patients with cancer from their institutions as well as from other agencies and associations with which they had affiliations. The guideline search strategy is provided in Appendix A of the original guideline document.

(b) Guideline Selection Criteria and Appraisal: Guidelines were selected for inclusion that were: (i) focused on antiemetic use for the prevention of acute AINV; (ii) based on a systematic review of the literature and (iii) published in English or French. Guidelines were excluded if it was not clear that the guideline statements or recommendations were based on a review of evidence from the literature and/or were not based on a source that used evidence to support the guideline development process.

Primary Literature Search for Pediatric Studies

As none of the guidelines identified specifically addressed antiemetic use for the prevention of acute AINV in children with cancer, a systematic review of primary pediatric oncology studies addressing this topic was conducted.

(a) Search Strategy: The following electronic databases were searched: Medline, Embase, CCTR, AMED, HTA, NHSEED and CINHAL. The search strategy including search terms and limits for these searches are provided in Appendix C. In addition to the results of the electronic database search, studies identified from the personal files of panel members and unpublished supplementary data from the research of panel members were evaluated for inclusion.

(b) Selection Criteria and Appraisal: Studies were included if: (i) they were published in full text (i.e. abstracts were excluded), (ii) they were published in English or French (iii) they reported pediatric data separately, (iv) it was possible to determine the emetogenicity of the antineoplastic therapy administered using the POGO classification guideline or an assessment provided by the study's author(s); (v) they provided an explicit or implicit definition of complete acute AINV response; and (vi) they reported the complete acute AINV response rate as a proportion or percentage. Citations were divided among panel members for screening for inclusion/exclusion. Full-text screening was performed for those citations identified as potentially relevant. Evidence summary tables were compiled and reviewed by two panel members before consideration by the panel.

(c) Meta-Analysis: A meta-analysis was undertaken to evaluate the contribution of each antiemetic agent or antiemetic regimen to complete AINV control. All outcomes were described as proportions; for example, the proportion of patients with complete control among a particular group. Each study was weighted by the inverse variance. Given the anticipation of heterogeneity between studies, a random effects model was used for all analyses. The meta-analysis was performed using Review Manager (RevMan) (Version 5.1.0, The Cochrane Collaboration, Oxford, England). Sub-groups were compared by evaluating heterogeneity across sub-group results.

Primary Literature Review of Pediatric Oncology Studies

A total of 1660 references were retrieved from 7 electronic databases. An updated search was performed through November 1, 2011 and panel members also reviewed their personal files for papers that met inclusion criteria. There were a total of 574 duplicates, 704 were excluded based on the title/abstract screen and 321 excluded after full text screening. There were 72 papers that met inclusion criteria (refer to flowchart in Appendix C in original guideline document).

Due to the lack of evidence identified with respect to pediatric experience with dronabinol, levomepromazine or methotrimeprazine in the initial search for primary literature, separate computerized literature searches were performed for these agents. No relevant papers were identified (see Appendix D in original guideline document).

Number of Source Documents

From the primary literature review of pediatric oncology studies there were 72 papers that met inclusion criteria (refer to flowchart in Appendix C of the original guideline document).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

High quality - Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality - Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality - Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality - Any estimate of effect is very uncertain

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Each guideline identified through the search (see Appendix A in original guideline document) was independently reviewed and scored by 3 to 4 members of the Pediatric Oncology Group of Ontario (POGO) antineoplastic-induced nausea and vomiting (AINV) Guideline Development Panel using the Appraisal of Guidelines for Research & Evaluation (AGREE) instrument. The domains assessed by this instrument include: scope and purpose; stakeholder involvement; rigor; clarity and presentation; applicability, and editorial independence. The domain scores and overall assessments of each reviewer were aggregated and presented for discussion at a panel meeting held by teleconference. The AGREE scores are presented in Appendix B of the original guideline document. The suitability of each guideline for adaptation using the ADAPTE7 process was discussed by the panel. Reasons to support or refute adaptation of each guideline were provided. Rigor and applicability scores were emphasized in the selection of a source guideline.

Identification and Appraisal of Existing Guidelines

The guideline search yielded 60 citations that were screened for inclusion. Thirteen guidelines that were either developed for use in adults and/or for use in children using were identified (see Appendix A in original guideline document) and assessed using the AGREE Instrument. The assessments are summarized in Appendix B of the original guideline document. Two guidelines were selected as the source guideline for adaptation of this guideline:

1. The American Society of Clinical Oncology Guidelines for Antiemetics in Oncology: Update 2006
2. Putting Evidence into Practice: Evidence-Based Interventions to Prevent, Manage, and Treat Chemotherapy-Induced Nausea and Vomiting (2007) by Tipton et al.

Using ADAPTE methods, the American Society of Clinical Oncology (ASCO) guideline was the primary document utilized as the framework for the development of guidelines for AINV prevention in pediatric cancer patients for pharmacological therapies. While the ASCO guideline does provide a general recommendation for prophylaxis in the pediatric setting, the focus of the guideline is on antiemetic use for adult cancer patients and it is in this capacity that the guideline is referenced as a source document. Tipton et al. was used as the framework for non-pharmacological interventions. Although the recommendations of the source guidelines are based on adult data, the advantages of these guidelines include the rigorous methodologies used in their development and their structure. When it became available, the 2011 update to the ASCO guideline was compared to the previous version. Since the 2011 recommendations did not differ substantially from those provided in the 2006 version with respect to the health questions of interest, the 2011 update was cited as the source guideline.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Guideline Development Panel

Pediatric Oncology Group of Ontario (POGO) identified antineoplastic-induced nausea and vomiting (AINV) as a key supportive care initiative in

2008 and the POGO AINV Guideline Development Group was formed in December 2008. Members were selected with a view to obtain interdisciplinary representation from several POGO institutions as well as content expertise. Experts who had published in the area of AINV in children or who had a current research interest in AINV or supportive care in cancer were invited to join the guideline development group. After the completion of the POGO Guideline for the Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients in July 2010, panel members were asked to confirm their willingness to continue as members of the panel tasked with the adaptation of a second guideline in this series. One member resigned while a new member was recruited.

Decision-Making Process for Formulation of the Recommendations

Therapeutic efficacy and safety were the primary determinants of recommendations made by the guideline development panel regarding antiemetic choice. In the event of contradictory information regarding therapeutic efficacy, the panel members took a conservative approach; that is, the more aggressive, comprehensive antiemetic prophylaxis would be recommended. This approach would be less likely to lead to breakthrough antineoplastic-induced nausea and vomiting (AINV) and would perhaps allow reduction of antiemetic prophylaxis, if desired, in a patient in whom AINV was well-controlled.

Decisions were taken through panel discussions and any differences in opinion were resolved by consensus. The quality of evidence and strength of recommendations were assessed using the system developed by Guyatt et al by one author (LLD) and confirmed through discussion by the remaining panel members. If consensus was unable to be reached on any matter, a decision was made by the majority of panel members by a vote.

The "Evidence Summary and Discussion" sections in the original guideline document provide additional information specific for each recommendation.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Strength of Recommendation	Benefit vs Risk and Burdens	Methodology	Implications
1A Strong recommendation, high quality evidence	Desirable effects clearly outweigh undesirable effects or <i>vice versa</i>	Evidence from well done randomized controlled trials (RCTs) or Exceptional observational studies	Apply to most patients in most circumstances Further research unlikely to change recommendation
1B Strong recommendation, moderate quality evidence	Desirable effects clearly outweigh undesirable effects or <i>vice versa</i>	Evidence from RCTs with some flaws in study or Very strong evidence from observational studies	Apply to most patients in most circumstances Further research might be helpful
1C Strong recommendation, poor quality evidence	Desirable effects clearly outweigh undesirable effects or <i>vice versa</i>	Evidence of at least one critical outcome from observational studies, case series or RCTs with flaws	Apply to most patients in many circumstances Further research would be helpful
2A Weak recommendation, high quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important flaws or Exceptionally strong evidence from observational studies	Best action may depend on circumstances or patient or society values Further research unlikely to change recommendation
2B Weak recommendation, moderate quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important flaws or Very strong evidence from observational studies	Best action dependent on patient circumstances or patient or society values Further research may change recommendation
2C	Desirable effects closely	Evidence of at least one critical	Other alternatives may be

Strength of Recommendation	Benefit vs Risk and Burdens	Methodology	Implications
Weak recommendation with poor quality evidence	balanced with undesirable effects	outcome from observational studies, case series or RCTs with serious flaws	equally reasonable Further research very likely to change recommendation

Cost Analysis

Costs related to antiemetic agents may increase as a result of this guideline. However, these costs are counter-balanced by potential reductions in admissions due to refractory antineoplastic-induced nausea and vomiting (AINV) and/or dehydration following antineoplastic therapy and improvement in the quality of life experienced by paediatric cancer patients during treatment.

See Appendix M: "Relative Acquisition Costs of Recommended Antiemetic Agents in Ontario at the Time of Guideline Development" in the original guideline document.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

External Review and Consultation Process

Who Was Asked to Review the Guideline?

Content expert review: Physicians, nurses and pharmacists with an active clinical and/or research interest in antineoplastic-induced nausea and vomiting were asked to review the draft guideline. Content reviewers who submitted a review were: Drs. C. Baggott, S. Grunberg, A-M Langevin, A. Orsey, R. Phillips, M. van der Wetering and D. Woods.

External stakeholder review: Physician, nurse and pharmacist members of Pediatric Oncology Group of Ontario (POGO) centres and their satellites and members of the POGO Supportive Care Committee were asked to review the draft guideline.

What Process Was Followed?

The willingness of potential content expert reviewers to review the guideline was determined by contacting them by telephone or e-mail. Once agreement was obtained, the draft guideline was sent both electronically and by courier along with instructions for the reviewer to complete a survey (see Appendix J in original guideline document).

Following the content expert review, the draft guideline and quick review summary were sent electronically to nurses, nurse practitioners, pharmacists and oncologists who practice in POGO satellites and tertiary centres together with a request to review the document using a survey (see Appendix K in original guideline document). Reviewers returned the completed survey by fax, mail or electronically.

Discussion of Feedback

The survey results were discussed in detail by the POGO antineoplastic-induced nausea and vomiting (AINV) Guideline Development Panel and a decision on each point was taken by consensus. When the decision of the panel was not unanimous, a revision was made if it was supported by at least 60% of the guideline development panel members. The comments of the expert reviewers led to revisions to the guideline as outlined in Table 4 of the original guideline document.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Improvements in the supportive care of children with cancer by offering a standardized, evidence-based approach to the prophylaxis of antineoplastic-induced nausea and vomiting (AINV), optimization of AINV control and provision of cost-effective antiemetic prophylaxis

Potential Harms

- Implementation of this recommendation may lead to administration of ondansetron or granisetron to many children who may not require them to experience complete antineoplastic-induced nausea and vomiting (AINV) control. However, since AINV is a known risk factor for uncontrolled AINV with future antineoplastic therapy, the panel believed that the cost/benefit of giving 5-HT3 antagonists, at least with the first course of antineoplastic therapy of low emetogenicity, was acceptable.
- The antiemetic activity of chlorpromazine has not been evaluated in combination with a 5-HT3 antagonist. Given the lack of evidence-based alternatives, the use of chlorpromazine for AINV prophylaxis in combination with either ondansetron or granisetron for children who truly cannot or will not receive dexamethasone may be considered. Its use strictly in the in-patient setting seems prudent based on its sedating and hypotensive properties.
- In studies, drowsiness (55%) and dizziness (36%) were the most common adverse effects attributed to nabilone.
- The concomitant use of ondansetron with agents known to prolong the QT interval should be undertaken with caution; ECG monitoring may be prudent.

Contraindications

Contraindications

- Several contemporary pediatric treatment protocols, brain tumor and acute myelogenous leukemia (AML) protocols for example, discourage or prohibit corticosteroids as antiemetic agents. In brain tumor patients, it is felt that corticosteroids may prevent adequate distribution of antineoplastic agents into the central nervous system while corticosteroids are a risk factor for fungal infection in AML patients. Other treatment protocols prohibit the use of corticosteroids as antiemetic agents since corticosteroids are already a component of the anti-tumor treatment regimen. Still others may not allow the use of corticosteroids simply so that both treatment groups remain uniform and one is not 'contaminated' by the use of corticosteroids for AINV control. Occasionally, families or patients refuse corticosteroid prophylaxis due to adverse effects such as aggressive behaviour or moodiness.
- The use of ondansetron and other 5-HT3 antagonist agents should be avoided in patients with congenital QT prolongation.

Qualifying Statements

Qualifying Statements

- The Pediatric Oncology Group of Ontario (POGO) Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients was developed by health care professionals using evidence-based or best practice references available at the time of its creation. The content of the guideline will change since it will be reviewed and revised on a periodic basis. Care has been taken to ensure accuracy of the information. However, every health care professional using this guideline is responsible for providing care according to their best professional judgment and the policies and standards in place at their own institution.
- The information contained in this document was prepared with care. However, any application of this material is expected to be based on judicious independent medical assessment in the context of individual clinical circumstances as well as institutional policies and standards of practice. POGO does not make any guarantees of any kind whatsoever with respect to the content or use or application of this guideline.

POGO disclaims any responsibility for the application or use of this guideline.

- Recommended antiemetic strategies are limited to those available in Canada at the time of guideline development.

Implementation of the Guideline

Description of Implementation Strategy

Implementation Considerations

The guideline development panel acknowledge that the antiemetic doses recommended in this guideline may not agree with the licensed doses in specific jurisdictions. This may create a barrier to the acceptance of the recommended doses. The doses recommended in this guideline are, however, congruent with the available published evidence.

This guideline offers a platform upon which individual clinicians and institutions may frame local recommendations. Each institution is encouraged to adapt this guideline to their local context. In this way, local values and the local availability of resources can inform the recommendations.

Users of this guideline are encouraged to incorporate the recommendations of the guideline into:

- Antineoplastic treatment protocols and road maps
- Institutional guidelines for selection of antiemetic agents for the prevention of acute antineoplastic-induced nausea and vomiting
- Pre-printed or electronic (e.g. computerized physician order entry [CPOE]) order sets that include antineoplastic agents

Tools for Application

An algorithm summarizing recommended antiemetic strategies based on the emetogenicity of the antineoplastic therapy being administered is presented in Appendix L of the original guideline document. The availability of the algorithm in an electronic format would likely be most readily accepted by clinicians since it would facilitate bedside decision-making as well as facilitate the incorporation of the guideline recommendations into pre-printed or electronic antineoplastic order sets. Development of these tools will be considered by Pediatric Oncology Group of Ontario (POGO) as part of the knowledge translation plan for this guideline.

Use of patient-report tools which assess the antineoplastic-induced nausea and vomiting (AINV) experienced by each patient would facilitate communication regarding the severity of AINV and individualization of antiemetic prophylaxis. Tools such as prospective diaries (paper and electronic) and retrospective surveys may be considered.

Organizational Barriers and Cost Implications

Organizational barriers to the acceptance and uptake of this guideline may include:

- Dismissal of recommendations based on the relative scarcity of robust paediatric supporting evidence
- Reluctance by some clinicians to use state-of-the-art antiemetic agents including corticosteroid agents
- Reluctance by some clinicians to dose some antiemetics as recommended based on concerns regarding toxicity or satisfaction with the performance of doses currently used
- Lack of access to recommended antiemetic agents. This will not be an issue in POGO centres and their satellites

The relative acquisition costs of the antiemetic agents recommended in this guideline in effect in Ontario at the time of guideline development are presented in Appendix M of the original guideline document. Drug costs are highly variable and subject to change. Clinicians adapting this guideline for use in their institution are encouraged to verify their local drug acquisition costs.

Key Review Criteria For Monitoring and/or Audit Purposes

Guideline acceptance and adherence may be monitored prospectively or retrospectively indirectly through audit of antiemetic selection. Patient response (level of AINV control) maybe monitored prospectively.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Dupuis LL, Boodhan S, Holdsworth M, Robinson PD, Hain R, Portwine C, O'Shaughnessy E, Sung L. Guideline for the prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer patients. Toronto (ON): Pediatric Oncology Group of Ontario (POGO); 2012. 199 p. [129 references]

Adaptation

This guideline has been broadly adapted with permission from the following two source guidelines:

- The "Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update" (Basch et al, 2011). The American Society of Clinical Oncology is not responsible in any way for the adaptation.
- The Oncology Nursing Society guideline "Putting evidence into practice: Evidence-based interventions to prevent, manage, and treat chemotherapy-induced nausea and vomiting" (Tipton et al, 2007). The Oncology Nursing Society is not responsible in any way for the adaptation.

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Guideline Committee

Pediatric Oncology Group of Ontario (POGO) Antineoplastic-Induced Nausea and Vomiting (AINV) Guideline Development Panel

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

The guideline development panel members had no conflicts of interest with respect to the development of this guideline. The guideline was developed independently from any funding body other than those listed below. All work produced by the Pediatric Oncology Group of Ontario (POGO) antineoplastic-induced nausea and vomiting (AINV) Guideline Development Panel is editorially independent of its funding agencies.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [Pediatric Oncology Group of Ontario \(POGO\) Web site](#)

Print copies available through Pediatric Oncology Group of Ontario (POGO), 480 University Avenue, Suite 1014, Toronto, Ontario, M5G 1V2, Canada.

Availability of Companion Documents

The following is available:

- Guideline for the prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer patients. Quick summary.

Electronic copies: Available in Portable Document Format (PDF) from the [Pediatric Oncology Group of Ontario Web site](#)

Patient Resources

None available

NGC Status

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